SCNN1A gene

sodium channel epithelial 1 alpha subunit

Normal Function

The *SCNN1A* gene provides instructions for making one piece, the alpha subunit, of a protein complex called the epithelial sodium channel (ENaC). The channel is composed of alpha, beta, and gamma subunits, each of which is produced from a different gene. These channels are found at the surface of certain cells called epithelial cells in many tissues of the body, including the kidneys, lungs, and sweat glands. The ENaC channel transports sodium into cells.

In the kidney, ENaC channels take sodium into cells in response to signals that sodium levels in the body are too low. From the kidney cells, this sodium is returned to the bloodstream rather than being removed from the body (a process called reabsorption). In addition to regulating the amount of sodium in the body, the flow of sodium ions helps control the movement of water in tissues. For example, ENaC channels in lung cells help regulate the amount of fluid in the lungs.

Health Conditions Related to Genetic Changes

pseudohypoaldosteronism type 1

At least a dozen mutations in the *SCNN1A* gene cause pseudohypoaldosteronism type 1 (PHA1). This condition typically begins in infancy and is characterized by low levels of sodium (hyponatremia) and high levels of potassium (hyperkalemia) in the blood and severe dehydration. In particular, *SCNN1A* gene mutations are involved in autosomal recessive PHA1, a severe form of the condition that does not improve with age.

Most mutations in the *SCNN1A* gene result in a shortened alpha subunit protein of the ENaC channel. Other mutations delete a small piece of DNA or change a single protein building block (amino acid) in the alpha subunit protein. *SCNN1A* gene mutations lead to reduced or absent ENaC channel activity. As a result, sodium reabsorption is impaired, leading to hyponatremia and other signs and symptoms of autosomal recessive PHA1. The reduced function of ENaC channels in lung epithelial cells leads to excess fluid in the lungs and recurrent lung infections.

other disorders

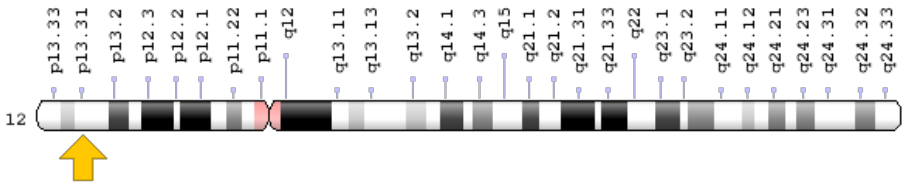
Some people with cystic fibrosis-like syndrome have a mutation or a normal gene variation (polymorphism) in the *SCNN1A* gene. People with cystic fibrosis-like syndrome (also known as atypical cystic fibrosis or bronchiectasis with or without

elevated sweat chloride type 2) have signs and symptoms that resemble those of cystic fibrosis, including breathing problems and lung infections. However, changes in the gene most commonly associated with cystic fibrosis, *CFTR*, cannot explain development of the condition. It is thought that a mutation or gene variation in the *SCNN1A* gene can disrupt sodium transport and fluid balance, which leads to the signs and symptoms of cystic fibrosis-like syndrome.

Chromosomal Location

Cytogenetic Location: 12p13.31, which is the short (p) arm of chromosome 12 at position 13.31

Molecular Location: base pairs 6,346,843 to 6,377,357 on chromosome 12 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- alpha-ENaC
- alpha-NaCH
- amiloride-sensitive epithelial sodium channel alpha subunit
- amiloride-sensitive sodium channel subunit alpha
- BESC2
- ENaCa
- ENaCalpha
- epithelial Na(+) channel subunit alpha
- FLJ21883
- nasal epithelial sodium channel alpha subunit
- nonvoltage-gated sodium channel 1 subunit alpha
- SCNEA
- SCNN1

- SCNNA_HUMAN
- sodium channel, non voltage gated 1 alpha subunit
- sodium channel, non-voltage-gated 1 alpha subunit
- sodium channel, nonvoltage-gated 1 alpha

Additional Information & Resources

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SCNN1A%5BTIAB%5D%29+OR+%28%28alpha-ENaC%5BTIAB%5D%29+OR+%28alpha-NaCH%5BTIAB%5D%29+OR+%28amiloride-sensitive+epithelial+sodium+channel+alpha+subunit%5BTIAB%5D%29+OR+%28ENaCa%5BTIAB%5D%29+OR+%28ENaCalpha%5BTIAB%5D%29+OR+%28SCNN1%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D

OMIM

- BRONCHIECTASIS WITH OR WITHOUT ELEVATED SWEAT CHLORIDE 2
  http://omim.org/entry/613021
- SODIUM CHANNEL, NONVOLTAGE-GATED 1, ALPHA SUBUNIT
  http://omim.org/entry/600228

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SCNN1A.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SCNN1A%5Bgene%5D
- HGNC Gene Family: Sodium channels epithelial
  http://www.genenames.org/cgi-bin/genefamilies/set/185
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=10599
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/6337
- UniProt
  http://www.uniprot.org/uniprot/P37088

Sources for This Summary

- Azad AK, Rauh R, Vermeulen F, Jaspers M, Korbmacher J, Boissier B, Bassinet L, Fichou Y, des Georges M, Stanke F, De Boeck K, Dupont L, Balascáková M, Hjelte L, Lebecque P, Radojkovic D, Castellani C, Schwartz M, Stuhrmann M, Schwarz M, Skalicka V, de Monestrol I, Girodon E, Férec C, Claustres M, Tümmler B, Cassiman JJ, Korbmacher C, Cuppens H. Mutations in the amiloride-sensitive epithelial sodium channel in patients with cystic fibrosis-like disease. Hum Mutat. 2009 Jul; 30(7):1093-103. doi: 10.1002/humu.21011.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19462466
- Canessa CM, Schild L, Buell G, Thorens B, Gautschi I, Horisberger JD, Rossier BC. Amiloride-sensitive epithelial Na+ channel is made of three homologous subunits. Nature. 1994 Feb 3; 367(6462):463-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8107805
- Chang SS, Grunder S, Hanukoglu A, Rösler A, Mathew PM, Hanukoglu I, Schild L, Lu Y, Shimkets RA, Nelson-Williams C, Rossier BC, Lifton RP. Mutations in subunits of the epithelial sodium channel cause salt wasting with hyperkalaemic acidosis, pseudohypoaldosteronism type 1. Nat Genet. 1996 Mar;12(3):248-53.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8589714
- Chen SY, Bhargava A, Mastroberardino L, Meijer OC, Wang J, Buse P, Firestone GL, Verrey F, Pearce D. Epithelial sodium channel regulated by aldosterone-induced protein sgk. Proc Natl Acad Sci U S A. 1999 Mar 2;96(5):2514-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10051674
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC26816/
- Masilamani S, Kim GH, Mitchell C, Wade JB, Knepper MA. Aldosterone-mediated regulation of ENaC alpha, beta, and gamma subunit proteins in rat kidney. J Clin Invest. 1999 Oct;104(7): R19-23.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10510339
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC408561/
- Mutesa L, Azad AK, Verhaeghe C, Segers K, Vanbellinghen JF, Ngendahayo L, Rusingiza EK, Mutwa PR, Rulisa S, Koulischer L, Cassiman JJ, Cuppens H, Bours V. Genetic analysis of Rwandan patients with cystic fibrosis-like symptoms: identification of novel cystic fibrosis transmembrane conductance regulator and epithelial sodium channel gene variants. Chest. 2009 May;135(5):1233-42. doi: 10.1378/chest.08-2246. Epub 2008 Nov 18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19017867
- OMIM: SODIUM CHANNEL, NONVOLTAGE-GATED 1, ALPHA SUBUNIT
  http://omim.org/entry/600228

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